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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/701,041	11/04/2003	Benjamin Oshlack	200.1133CON2	6154

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EXAMINER
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ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/701,041	OSHLACK ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62-74* is/are pending in the application.

4a) Of the above claim(s) *68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62-67 and 69-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/4/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :3/28/07; 12/26/07; 5/22/08; 11/4/03.

DETAILED ACTION

Claims 62-74 are pending. Applicants previously cancelled claims 1-61 in a preliminary amendment. Applicants have amended claims 66 and 70. Claim 68 is withdrawn from consideration as being drawn to a non-elected species. **Claims 62-67 and 69-74 are under consideration in the instant office action**. Receipt and consideration of Applicants' IDS's (submitted 3/28/08; 5/22/08; and 11/4/03), amended claim set, and remarks/arguments submitted on February 1, 2008 are acknowledged. All rejections/objections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments, specification amendments, and/or persuasive arguments.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 12/26/07, 3/28/08; and 5/22/08 have been considered by the examiner. The file of the parent of the instant application (Application No. 09/781,081; now U.S. Patent No. 6,696,088) has been reviewed and the previously unconsidered foreign patents and non-patent literature references originally cited on the IDS submitted on November 4, 2003 were reviewed and considered. A clean copy of the November 4, 2003 IDS, which has been newly signed and dated, is provided with the instant office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 62-67 and 69-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palermo (WO 99/32120) ("Palermo"; IDS reference) in view of Elger et al. (U.S. Pat. No. 4,844,907) ("Elger"; IDS reference).

Applicant Claims

Applicants claim (1) a composition comprising (i) an inert core, (ii) a fist layer, and (iii) a second layer, the first layer being located between the core and the second layer, and the second layer consisting essentially of an opioid antagonist (e.g. naltrexone) and the second layer a hydrophobic material and (2) an oral dosage form comprising an opioid agonist (e.g. oxycodone) and the composition of claim 62 (i.e. composition (1), as described above).

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Palermo (WO '120) teaches an **oral dosage form of an opioid analgesic, comprising an analgesically effective amount of an opioid agonist together with an opioid antagonist**, the amount of opioid antagonist including being sufficient to counteract opioid effects if extracted together with the opioid agonist (see p. 6, lines 1-18). In certain preferred embodiments, **the opioid agonist is** hydrocodone, hydromorphone, **oxycodone**, morphine or pharmaceutically acceptable salts thereof (p. 7, lines 5-6). **Suitable opioid antagonists disclosed include naltrexone**, naloxone, nalmephene, cyclazocine and levallorphan. A most preferred antagonist is naltrexone (p. 11, lines 14-19); (p. 13, lines 14-31). In certain preferred embodiments of the method, the opioid agonist and the opioid antagonist are combined in a ratio of opioid antagonist to opioid agonist which is analgesically effective when the combination is administered orally, but which is aversive in a physically dependent subject (p. 7, lines 7-15). In embodiments where the opioid is hydrocodone and the antagonist is naltrexone, the ratio of naltrexone to hydrocodone is preferably from about 0.03-0.27:1 by weight (p. 7, lines 15-26). Palermo teaches that the dosage forms of the invention may be liquids, tablets, multiparticulates, dispersible

powders or granules, hard or soft capsules, lozenges, aqueous or oily suspensions, emulsions, syrups, elixirs, microparticles, buccal tablets, etc. (p. 7, lines 27- 31); (p. 8, line 29 - p. 9, line 1). In certain preferred embodiments, the oral dosage forms are sustained release formulations. This may be accomplished via the incorporation of a sustained release carrier into a matrix containing the opioid agonist and opioid antagonist; or via a sustained release coating of a matrix containing the opioid agonist and opioid antagonist, where the sustained release coating contains at least a portion of the sustained release carrier included in the dosage form (p. 8, lines 1-9); (p. 20, lines 16-21).

With regards to ratios, Palermo teaches that the combinations of opioid antagonists/opioid agonists which are orally administered in ratios which are equivalent to the ratio of e.g., naltrexone to hydrocodone set forth are considered to be within the scope of the invention. For example, in some embodiments, naloxone is utilized as the opioid antagonist, the amount of naloxone included in the dosage form being large enough to provide an equiantagonistic effect as if naltrexone were included in the combination (p. 19-31). This demonstrates bioequivalency of the dosage forms. Palermo teaches that the dosage forms may be coated with one or more materials suitable for the regulation of release or the protection of the formulation. The coatings are provided to permit either pH-dependent or pH-independent release (p.21, lines 18-29). In preferred embodiments, the substrate (e.g., **tablet core bead**, matrix particle) containing the opioid analgesic **is coated with a hydrophobic material** selected from (i) an alkylcellulose; (ii) an acrylic polymer or (iii) mixtures thereof (p. 22, lines 6-14). Suitable and preferred alkylcellulose polymers taught include ethylcellulose (p. 22, lines 19-25). Acrylic polymers are also disclosed and include acrylic acid and methacrylic acid copolymers,

methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, poly(acrylic acid), poly(methacrylic acid) and the like (p. 23, line 10 - p. 24, line 22); (p. 29, lines 7-18). Plasticizers can also be included in the composition (p. 24, line 24 - p. 25, line 20). **A process for preparing coated beads is disclosed at p. 25, line 21 - p. 28, line 8**. Matrix bead formulations are disclosed at page 28. Hydrophilic and/or hydrophobic materials, such as gums, cellulose ethers, acrylic resins, protein derived materials and any pharmaceutically acceptable hydrophobic material or hydrophilic material, which is capable of imparting, controlled release of the active agent and which melts (or softens to the extent necessary to be extruded) may be used in this invention (p. 28, lines 19-30).

With regards to amounts of hydrophobic material claimed, the Examiner notes that suitable or effective amounts can be determined by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results as these are variable parameters attainable within the art. Moreover, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. The Palermo reference explicitly recognizes and teaches oral dosage forms comprising opioid agonists in combination with opioid antagonists, whereby the dosage forms are effective for the substantial reduction of pain.

Elger et al. ('907) teach a pharmaceutical composition for the treatment of pain comprising a narcotic analgesic and a non-steroidal anti-inflammatory drug, whereby **the composition is in the form of a multi-phase, layered tablet, especially bi-layered tablet (see reference column 1, line 1 - col. 2, line 3 and Abstract)**. Suitable narcotic analgesics disclosed include hydrocodone, morphine and codeine (see Table at column 2).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Palermo does not explicitly teach layered dosage forms. This deficiency is cured by the teachings of Elger.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the layered dosage forms of Elger et al. within the formulations of Palermo. One of ordinary skill in the art would do so because Elger et al. teach layered pharmaceutical compositions comprising narcotic analgesics and teach that the layered dosage forms (i.e., bi-layered dosage forms) provide for separation of different drugs or phases. The expected result would be an improved multi-layered dosage formulation for the effective treatment of pain. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Applicants' data as depicted in Figures 1-3 in the specification is noted. Applicants' data is not deemed to demonstrate unexpected results. Therefore, the claimed invention, as a whole, would have been

prima facie obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 63 and 71-72 **remain provisionally rejected** on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 48, 51, and 56 of copending Application No. 10/389,238 (copending '238) for the reasons of record, which have been restated below.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the cited claims of both applications are substantially overlapping in scope and mutually obvious. Independent claim 62 of the instant application has been described above

in the instant office action. Independent claim 48 of copending '238 claims a pharmaceutical composition comprising (i) an inert core, (ii) a 1st layer, and (iii) a 2nd layer, the 1st layer being between the core and the 2nd layer and comprising a mixture of naltrexone hydrochloride and a stabilizer, and the second layer comprising a hydrophobic material. Independent claim 51 of copending '238 claims a pharmaceutical composition comprising a 1st component comprising about 10 mg of oxycodone hydrochloride and a 2nd component comprising less than about 5.0 mg naltrexone hydrochloride and a stabilizer, wherein said 2nd component comprises a plurality of substrates comprising a mixture of naltrexone hydrochloride and stabilizer. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 63 and 71-72 of the instant application *prima facie* obvious over claims 48, 51, and 56 of copending Application No. 10/389,238 (copending '238).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 62-63 **remain provisionally rejected** on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 41 of copending Application No. 10/401,111 (copending '111) for the reasons of record, which have been restated below.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the cited claims of both applications are substantially overlapping in scope and mutually obvious. Independent claim 62 of the instant application has been described above in the instant office action. Independent claim 41 of copending '111 an oral dosage form comprising (i) an inert core, (ii) a 1st layer, and (iii) a 2nd layer, the 1st layer being between the

core and the 2nd layer and comprising a mixture of naltrexone hydrochloride and a stabilizer, and the second layer comprising a mixture of gelatin and a hydrophobic material. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 62-63 of the instant application *prima facie* obvious over claim 41 of copending Application No. 10/401,111 (copending '111).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 62-64 **remain provisionally rejected** on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-3 and 15-17 of copending Application No. 10/524,334 (copending '334) for the reasons of record, which have been restated below.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the cited claims of both applications are substantially overlapping in scope and mutually obvious. Independent claim 62 of the instant application has been described above in the instant office action. Independent claim 1 of copending '334 an oral dosage form comprising (i) a substrate comprising an opioid antagonist (e.g. an inert core, such as is recited in claims 2-3 of copending '334) (ii) a diffusion barrier coating comprising an anionic polymer over said substrate layer, and (iii) a coating comprising a hydrophobic material coated over said diffusion barrier coating. Dependent claims 15-16 of copending '334 further specify the nature of the coating material as being a hydrophobic material that provides sequestration of the opioid antagonist. Dependent claim 17 of copending '334 claims the pharmaceutical formulation of claim 1, wherein the opioid antagonist is selected from the group consisting of naltrexone,

naloxone, and pharmaceutically acceptable salts thereof. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 62-64 of the instant application *prima facie* obvious over claims 2-3 and 15-17 of copending Application No. 10/514.334 (copending '334).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments to All Outstanding Obviousness-Type Double Patenting Rejections

Applicant's arguments filed 2/1/2008 have been fully considered but they are not persuasive. Applicants have not provided any substantive arguments traversing the above-maintained provisional obviousness-type double patenting rejection, but have merely stated an intention to consider filing terminal disclaimers upon indication that the claims are allowable. Thus, the above rejections are maintained at this time, because no substantive arguments were presented traversing these rejections.

Conclusion

Claims 62-67 and 69-74 are rejected. No claims under consideration in the instant office action are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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